Nature, Structures and Synthetic Organic Chemistry

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I became an organic chemist to avoid physical chemistry. I also became engaged in organic structural studies and bioorganic chemistry rather than synthetic chemistry due to a careless error in performing my very first undergraduate organic reaction. It is now ironic to find myself writing this article for the current English edition that deals with synthetic organic chemistry.

My first exposure to "organic synthesis (?)" happened as follows.

I entered Nagoya University in September 1944, the time just before the end of World War II in August 1945. University laboratories were dispersed into the countrysides to avoid damage. Our first year class joined the group of Professor Fujio Egami and Assistant Professor Yoshimasa Hirata, went to Ueda, a poetic town near the Japanese Alps, and stayed in the dormitories of Ueda Sericulture College (the current Shinshu University).

We were supposedly involved in assisting the research for the armory at Hiratsuka naval base. Despite our total lack of undergraduate organic labor work except for the meager exposure during wartime high school life, my first and last assignment was the preparation of ethylene oxide from ethylene chlorohydrin. A 5 liter three-neck flask, brought painstakingly from Nagoya in a fully packed train, containing several grams of the chlorohydrin in the bottom of the big flask was heated, and to this was added aqueous sodium hydroxide from the side funnel. As soon as the cold aqueous base solution hit the wall of the warm wall, the wall cracked. This was the end of the elaborate setup of my first organic reaction. No more flasks were left and I was sent back to Nagoya to fetch more equipment. Ever since, I have had some psychological barrier in preparative organic chemistry.

Structure determination of natural products started with the isolation of whatever one could isolate. In the pre-spectroscopic era, some structure determinations, coupled with degradations and derivatizations, would take 20-30 years, and were like solving a mystery. This picture is now replaced by assay guided isolation and spectroscopy, with less degradations; subsequent progress has reduced the time and quantity needed so that lower microgram scale structure determinations are not unusual. A major difference between structure determination and synthetic chemistry is that the role of memory is minor in the former, whereas it is central in the latter. Isolation requires careful manipulations and experience, especially when dealing with minuscule amounts of sensitive material. Although spectroscopy seldom requires memory, its imaginative use leads to new general protocols. Combined use and interpretation of various spectroscopic methods, coupled with the rapidly advancing theoretical treatment of spectral data, continues to contribute to the advancement in structural clarifications. It is now becoming possible to clarify even the nature of physiological activity, namely the static and time-resolved structural interactions between the bioactive ligand and receptors.